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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2200798-W00	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IL03/00508	International filing date (day/month/year) 13 June 2003 (13.06.2003)	Priority date (day/month/year) 14 June 2002 (14.06.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61N 1/00 and US Cl.: 607/1		
Applicant BRAINSGATE LTD.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u> </u> sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 14 January 2004 (14.01.2004)	Date of completion of this report 11 September 2004 (11.09.2004)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer <i>Sharon H. Greene for</i> Kristen Mullen (formerly Droesch) Telephone No. 703-605-1185	

I. Basis of the report**1. With regard to the elements of the international application:***

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-95 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages 96-126, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the drawings:
pages 1-12, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)	Claims <u>1-163</u>	YES
	Claims <u>164-177</u>	NO
Inventive Step (IS)	Claims <u>1-163</u>	YES
	Claims <u>164-177</u>	NO
Industrial Applicability (IA)	Claims <u>1-177</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Please See Continuation Sheet

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Claims 164-177 lack novelty under PCT Article 33(2) as being anticipated by Hayes et al. (6,325,475).

With respect to claims 164-173, Hayes et al. shows an apparatus comprising an odorant storage vessel (212), an odorant, and an odorant delivery element (214, 216, 202) comprising an aqueous spray inhaler, or air dilution olfactometer adapted to present the odorant to the nasal cavity and throat (Fig. 2; Col. 9-line 20-Col. 10, line 7).

Regarding claims 175-177, Hayes et al. shows the odorant comprises amyl acetate, acetic acid, citric acid, menthol, and alcohol (Col. 19, line 14- Col. 20, line 46).

Claims 164-174 lack novelty under PCT Article 33(2) as being anticipated by Hayes et al. (6,338,715). Hayes et al. show an apparatus comprising an odorant storage vessel (7), an odorant, and an odorant delivery element (6,9,10,11) comprising an aqueous spray inhaler, or air dilution olfactometer adapted to present the odorant to the nasal cavity and throat.

Claims 1-163 meet the criteria set out in PCT Article 33(2)-(3).

Regarding claims 1-18, 77-78, 89-104, 145-146, and 157-163, the prior art does not teach or fairly suggest a method or apparatus adapted for treating Alzheimer's comprising stimulating the sphenopalatine ganglion related tissue of a subject by applying an electrical signal to the tissue or by presenting an odorant to an air passage of the subject, and configuring the stimulation to cause an increase in clearance of an Alzheimer's related constituent of from cerebrospinal fluid or the brain to systemic blood circulation.

With respect to claims 19-46, 79-80, 89-95, 105-114, 147-148, and 157-163, the prior art does not teach or fairly suggest a method or apparatus adapted for treating Alzheimer's comprising providing a pharmaceutical agent into the systemic blood circulation of the subject; stimulating the sphenopalatine ganglion related tissue of a subject by applying an electrical signal to the tissue or by presenting an odorant to an air passage of the subject, and configuring the stimulation to cause an increase in passage of the pharmaceutical agent from the systemic blood circulation into the central nervous system

Regarding claims 47-50, 81-82, 89-95, 115-118, 149-150, and 157-163, the prior art does not teach or fairly suggest a method or apparatus adapted for treating Alzheimer's comprising stimulating the sphenopalatine ganglion related tissue of a subject by applying an electrical signal to the tissue or by presenting an odorant to an air passage of the subject, and configuring the stimulation to cause an increase in cerebral blood flow.

With respect to claims 51-58, 83-84, 89-95, 119-126, 151-152, and 157-163, the prior art does not teach or fairly suggest a method or

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

apparatus adapted for treating Alzheimer's comprising stimulating the sphenopalatine ganglion related tissue of a subject by applying an electrical signal to the tissue or by presenting an odorant to an air passage of the subject, and configuring the stimulation to cause an increase in molecular passage between the central nervous system and another body compartment.

Regarding claims 59-76, 85-93, 127-144, 153-163, and 157-163, the prior art does not teach or fairly suggest a method or apparatus adapted for treating Alzheimer's comprising stimulating the sphenopalatine ganglion related tissue of a subject by applying an electrical signal to the tissue or by presenting an odorant to an air passage of the subject, and configuring the stimulation to cause an increase in molecular passage between the cerebrospinal fluid and another body fluid or tissue of the subject.

Claims 1-177 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry.

----- NEW CITATIONS -----